

## Radiological deterioration worsens despite clinical improvement in rheumatoid arthritis

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**Title:** Clinical improvement and radiological deterioration in rheumatoid arthritis: Evidence that the pathogenesis of synovial inflammation and articular erosion may differ

**Source:** *Br J Rheumatol* 1996; 35: 1263-8.

**Aim:** A striking discrepancy between clinical improvement and radiological deterioration has been observed in rheumatoid arthritis (RA). This study investigates the relationship between clinical and laboratory measures of disease activity and the radiological course in a cohort of RA patients.

**Methods:** 57 patients with active RA who had not previously been taking any disease modifying drug (DMARD) or oral or intra-articular corticosteroids (CS) entered a prospective study in which they were assessed at enrollment and their condition was reviewed after an observation period of 6 years. At the time of review patients completed an Arthritis Impact Measurement Scale (AIMS) questionnaire. At entry and at review, six clinical and laboratory variables were used to assess disease activity: (1) duration of morning stiffness (MS) on a 1-4 scale; (2) pain on a 10 cm visual analogue scale; (3) grip strength; (4) the Ritchie index (RI); (5) a full blood count (hemoglobin); and (6) the erythrocyte sedimentation rate (ESR). Current non-steroidal anti-inflammatory drug (NSAID), CS or DMARD therapy and previous DMARD therapy since enrollment were documented at review. X-rays of the hands and feet were obtained at enrollment and at review: articular damage was quantified according to the Larsen method by a blinded observer. The radiological course was measured either by actual changes in the radiological score, or by a standardized percentage change. For the statistical analysis, two-sample or paired T-tests and simple regression were used.

**Results:** 40 out of the 57 patients originally enrolled attended the review: 73% were taking NSAIDs, 43% oral GC and 70% a DMARD. At review, the RA AIMS scores were higher than those reported in a cohort of healthy subjects, and all of the disease activity measures improved significantly ( $P < 0.0001$ ), i.e.: ESR in  $> 90\%$  patients; RI, MS, GS in  $> 80\%$  patients, and hemoglobin levels rose in 75% patients.

39 patients had X-rays taken at review and 30 patients had serial X-rays (enrollment and review). The mean radiological score deteriorated significantly between enrollment and review ( $P < 0.0001$ ). No correlation was found between any of the measures of disease activity at the time of enrollment and the change in articular damage during the period of observation. Correlations were observed between some of the measures of disease activity at the time of review and the radiological course: RI, hemoglobin and ESR correlated with both the ac-

tual and the standardized change in the radiological scores and with the degree of articular erosion at the time of review. RI, hemoglobin and ESR significantly reflected the radiological outcome ( $r = 0.0.36, -0.44$  and  $0.36$ , respectively)

**Conclusions:** Articular erosion worsens in RA despite clinical improvement and is accelerated in those patients with evidence of persistent synovial inflammation, as reflected in the clinical and laboratory measures of disease activity. This could reflect a potentially different pathogenetic process of articular erosion and synovitis.

### Comment

*This manuscript presents evidence that patients may improve over 6 years in disease activity measures such as joint tenderness and the erythrocyte sedimentation rate, while experiencing radiographic progression over the same time period. Similar findings have been documented in 3 other studies of the course of rheumatoid arthritis over 5 years or longer (1-3). This study illustrates several important principles for clinical research in rheumatoid arthritis: 1. Long term studies which include only measures of inflammation such as joint swelling without measures of damage such as joint deformity (4) may be insensitive to detection of the true progression of disease, as damage may progress while inflammation is under control. 2. Partial control of inflammation may not necessarily prevent radiographic progression, raising questions about goals of a 20% or even a 70% response (5) as valid treatment goals. 3. Accurate, evidence-based description of the course of rheumatoid arthritis and responses to therapies is not possible from clinical trials over less than 3 years (the duration of the longest clinical trial in rheumatoid arthritis - most are less than one year), but requires long-term observational studies.*

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